

Fig. 1A DNA and Amino Acid Sequence of Variable Region of FR1-H7 Heavy Chain

Heavy chain variable region sequence (cDNA)

```
ATGGCCGAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGG
GCCTCAGTGAAGGTTCTGCAAGGTTCTGGATAACACCTTCACCGACTACTA
CATGCACGGGTGCAACAGGCCCTGGAAAAGGGCTTGAGTGGATGGGACTT
GTTGATCCTGAAGATGGTAAACAATCTACGCAGAGAAGTTCCAGGGCAGAG
TCACCATAACCGCGGACACGTCTACAGACACAGCCTACATGGAGCTGAGCAG
CCTGAGATCTGAGGACACGCCGTGTATTACTGTGCGAGAGATGACTACATG
GACGTCTGGGCAAAGGCACCCCTGGTCACCGTCTCAAGCGCCTCCACCAAGG
GCCCA
```

Heavy chain variable region sequence (amino acid)

```
MAEVQLVQSGAEVKKPGASVKVSCKVSGYTFDYYMHWVQQAPGKGLEWMG
LVDPEDGE TIYAEKFQGRVTITADTSTDAYMELSSLRSEDTAVYYCARDDYMD
VWGKGTL VTVSSASTKGP
```

Fig. 1B DNA and Amino Acid Sequence of Variable Region of FR1-H7 light Chain

Light chain variable region sequence (cDNA)

CTTGAAACGACACTCACGCAGTCTCCAGACACCCGTCTTGTCTCCAGGAGA
AGGAGCCACCCTCTCCTGTAGGGCCAGTCAGAGTGTAGCGGCAGTGCCTTG
GCCTGGTACCAAGCAGAAACCTGGCCAGGCTCCAGACTCCTCATCTATGATG
CATCCAGTAGGGCCACTGGCGTCCCAGACAGGTTCAGTGGCAGTGGGTCTGG
GGCAGACTTCAGTCTCACCATCAGCAGACTGGAGCCTGAAGATTTGCAGTG
TATTCCCTGTCAGCAATATGGTAGCTCACCTCTCACTTCGGCCCTGGGACCAA
AGTGGATGTCAAACGAACTGTGGCTGACCATCTGTCTCATCTTCCCGCCAT
CTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGCCTGCTGAATAAC
TTCTATCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATT

Light chain variable region sequence (amino acid)

LETTLTQSPDTLSLSPGEGATLSCRASQS VSGS ALAWYQQKPGQAPRLLIYDASS
RATGVPDRFSGSGSGADFSLTISLEPEDFAVYSCQQYGSPLTFGPGTKVDVKR
TVAAPSVFIFPPSDEQLKSGTASVVCLNNFYPREAKVQWKVD

Fig. 1C CDRs For FR1-H7 Nucleic Acid Sequences

VH (human heavy chain subclass I)

CDR1 GACTACTACATGCAC
CDR2 CTTGTTGATCCTGAAGATGGTAAACAATCTACGCAGAGAAGTTCCAGGGC
CDR3 GATGACTACATGGACGTC

VL (human kappa light chain subgroup III)

CDR1 AGGGCCAGTCAGAGTGTAGCGGCAGTGCCTGGCC
CDR2 GATGCATCCAGTAGGCCACT
CDR3 CAGCAATATGGTAGCTCACCTCTCACT

Fig. 1D CDRs For FR1-H7 Amino Acid Sequences**VH (human heavy chain subclass I)**

CDR1	DYYMH
CDR2	LVDPEDGETIYAEKFQG
CDR3	DDYMDV

VL (human kappa light chain subgroup III)

CDR1	RASQSVSGSALA
CDR2	DASSRAT
CDR3	QQYGSSPLT

Fig. 2A DNA and Amino Acid Sequence of Variable Region of FR1-A1 Heavy Chain**Heavy chain variable region sequence (cDNA)**

```
ATGGCCCAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGT
CCTCGGTGAAGGTCTCCTGCAAGGCTCTGGATCGACCTTCACCGGCTACTAT
ATGCACCTGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTGGATGGGAAGG
ATCATCCCTATCCTTGGTATAGCAAACATCGCACAGAACGTTCCAGGGCAGAG
TCACGATTACCGCGGACAAATCCACGAGCACAGCCTACATGGAGCTGAGCAG
CCTGAGATCTGAGGACACGGCCGTGTACTACTGTGCGAGAGGGAGGAGATCTG
GGCGGTATGGACGTCTGGGGCCAAGGGA
```

Heavy chain variable region sequence (amino acid)

```
MAQVQLVQSGAEVKKPGSSVKVSCKASGQFTGYYMHWVRQAPGQGLEWMG
RIIPILGIANYAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCARGGDLGG
MDVWGQG
```

Fig. 2B DNA and Amino Acid Sequence of Variable Region of FR1-A light Chain**Light chain variable region sequence (cDNA)**

CTTGAAATTGTGCTGACTCAGTCTCCACTCTCCCTGCCGTACCCCTGGAGA
GCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCCTCCGGCATAGTAATGGA
TACAACATATTGGATTGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT
GATCTATTGGCTTCTAATCGGGCCTCCGGGGTCCCTGACAGGTTCAGTGGCA
GTGGATCAGGCACAGATTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGA
TGTTGGGGTTATTACTGCATGCAAGCTACAAATCCTCCGACTTCGGCC
CTGGGACCAAGTGGATATCAAACGAACGTGGCTGCA

Light chain variable region sequence (amino acid)

LEIVLTQSPLSLPVTPGEPASISCRSSQSLRHSNGNYLDWYLQKPGQSPQLIYL
ASN RASGV PDRFSGSG TDFTL KISR VEAEDVGVYYCMQALQIPPTFGPGTKVD
IKRTVAA

Fig. 2C CDRs For FR1-A1 Nucleic Acid Sequences

VH (human heavy chain subclass I)

CDR1 GGCTACTATATGCAC

CDR2 AGGATCATCCCTATCCTTGGTATAGCAAACCTACGCACAGAAGTTCCAGGGC

CDR3 GGAGGAGATCTGGCGGTATGGACGTC

VL (human kappa light chain subgroup II)

CDR1 AGGTCTAGTCAGAGCCTCCGGCATAGTAATGGATACAACATTGGAT

CDR2 TTGGCTTCTAATCGGGCTCC

CDR3 ATGCAAGCTCTACAAATTCCCTCCGACT

Fig. 2D CDRs For FR1-A1 Amino Acid Sequences

VH (human heavy chain subclass I)

CDR1	GYYMH
CDR2	RIIPILGIANYAQKFQG
CDR3	GGDLGGMDV

VL (human kappa light chain subgroup II)

CDR1	RSSQSLRHSNGNYLD
CDR2	LASNKRAS
CDR3	MQALQIPPT

Fig. 3

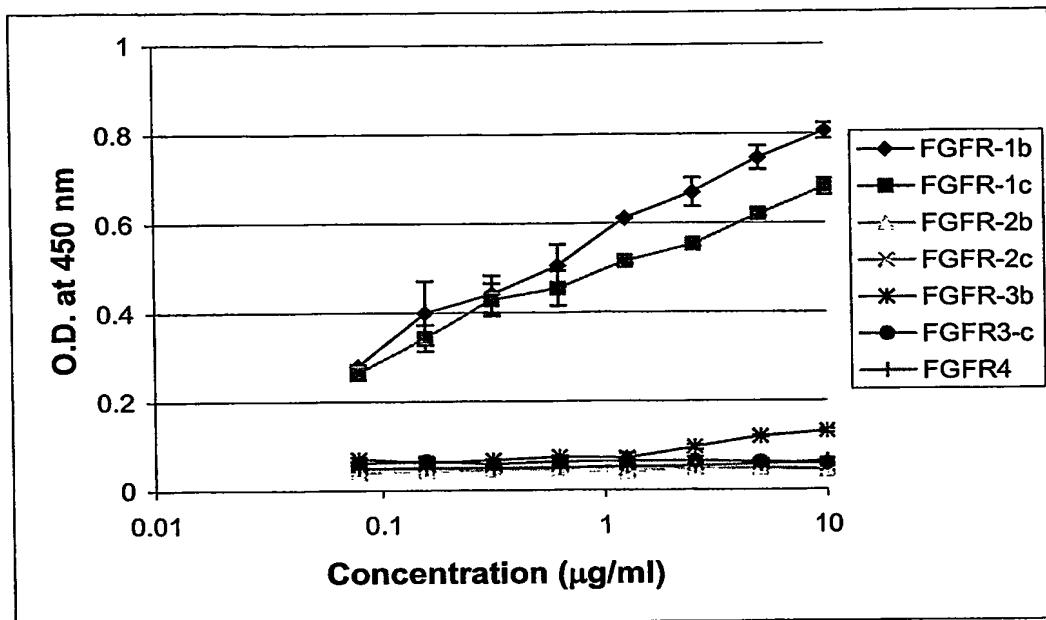


Fig. 4A

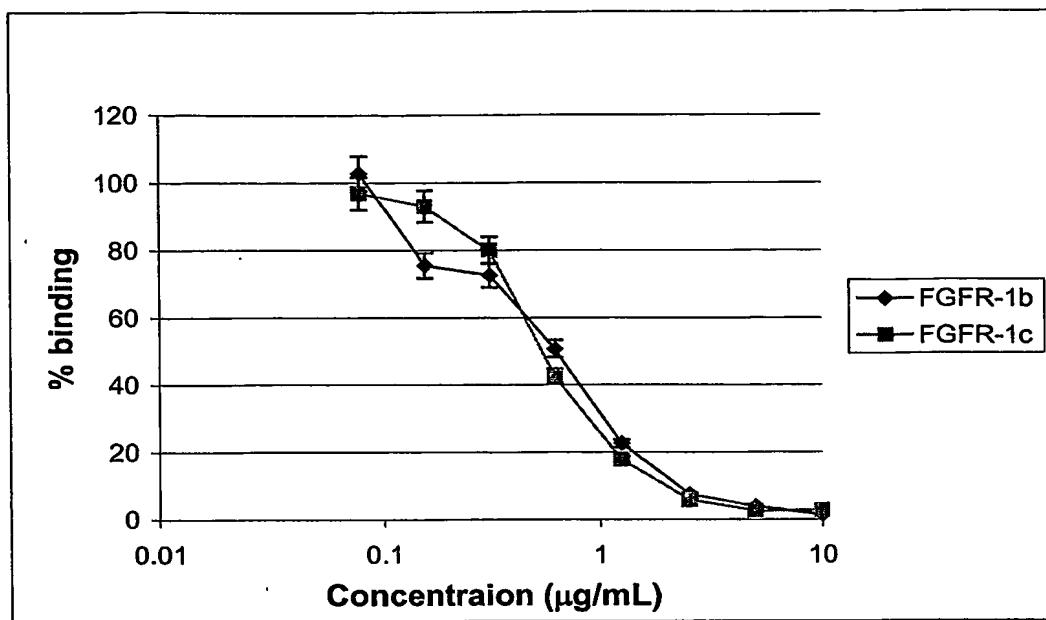


Fig. 4B

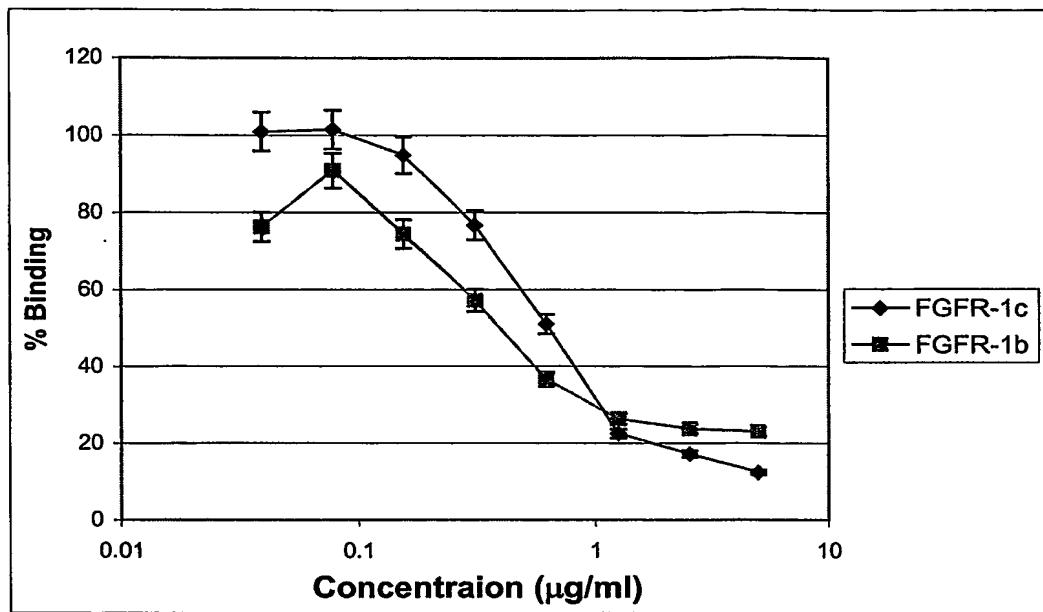


Fig. 5A

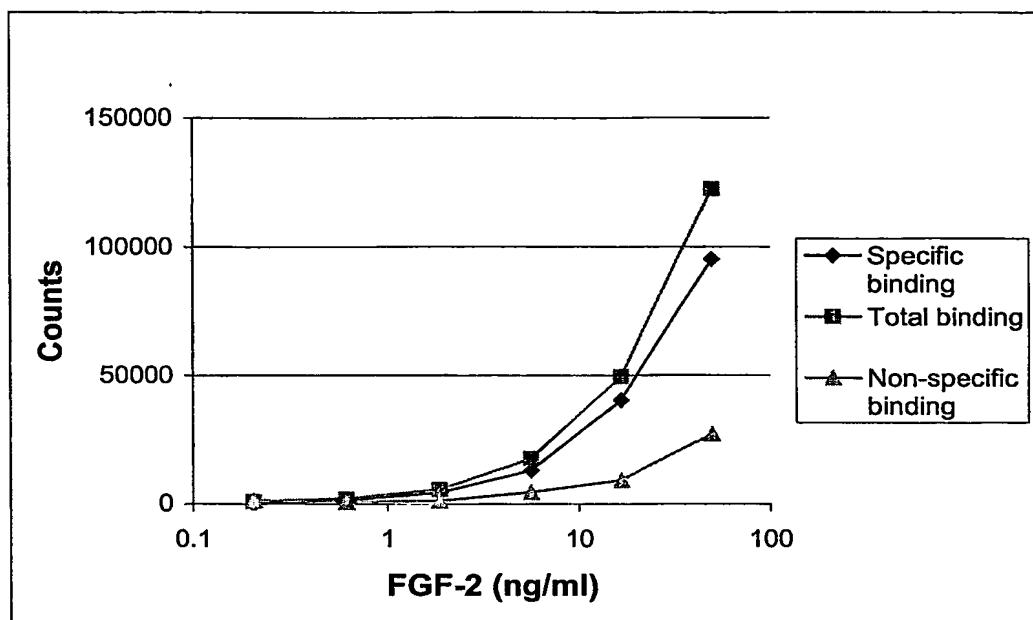


Fig. 5B

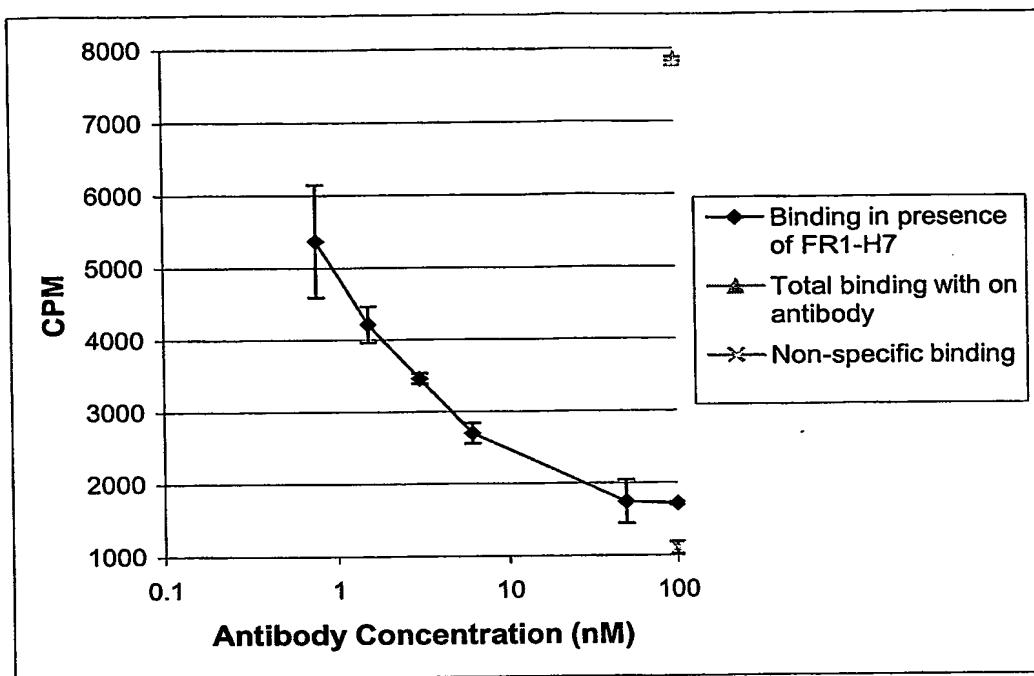


Fig. 6

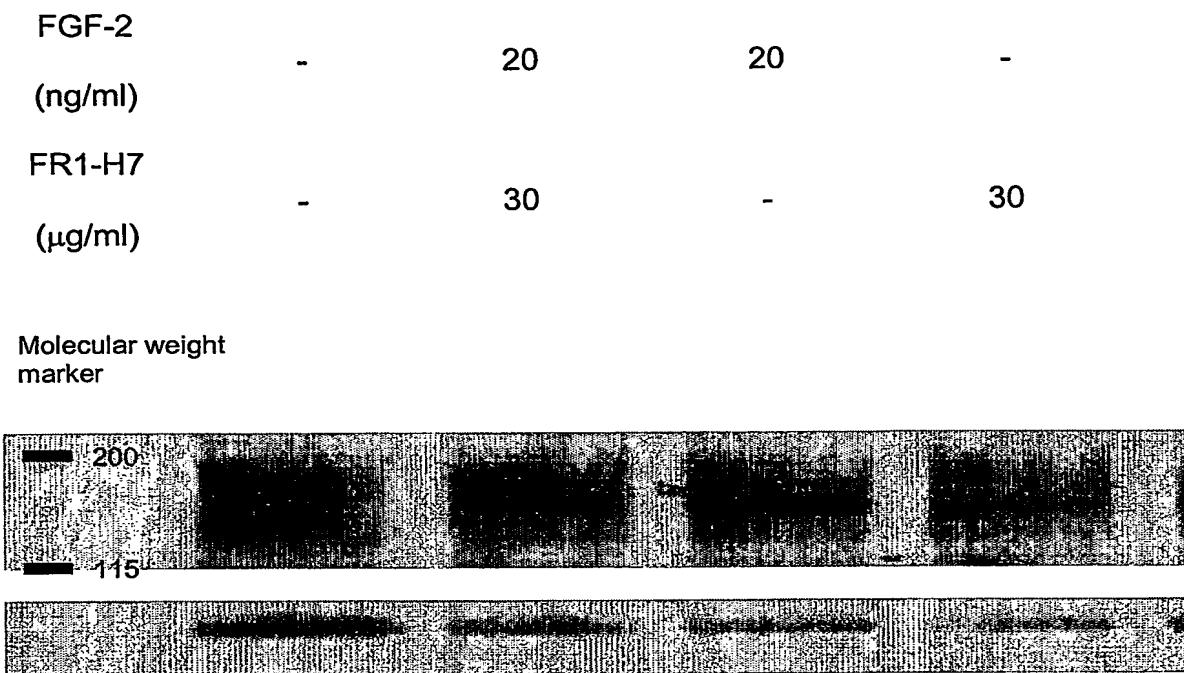


Fig. 7

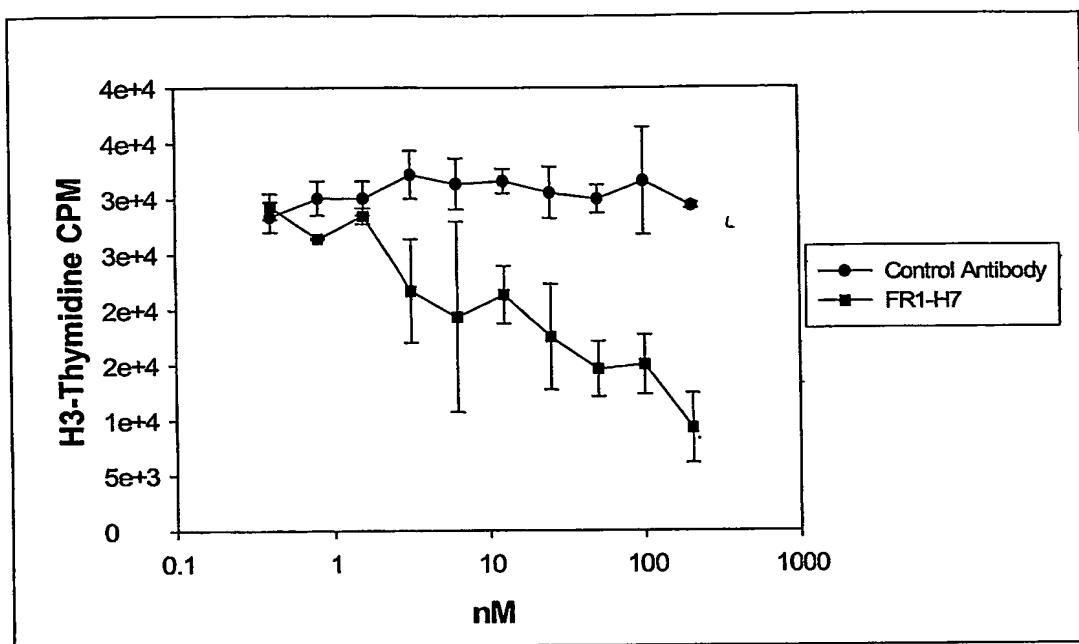


Fig. 8A

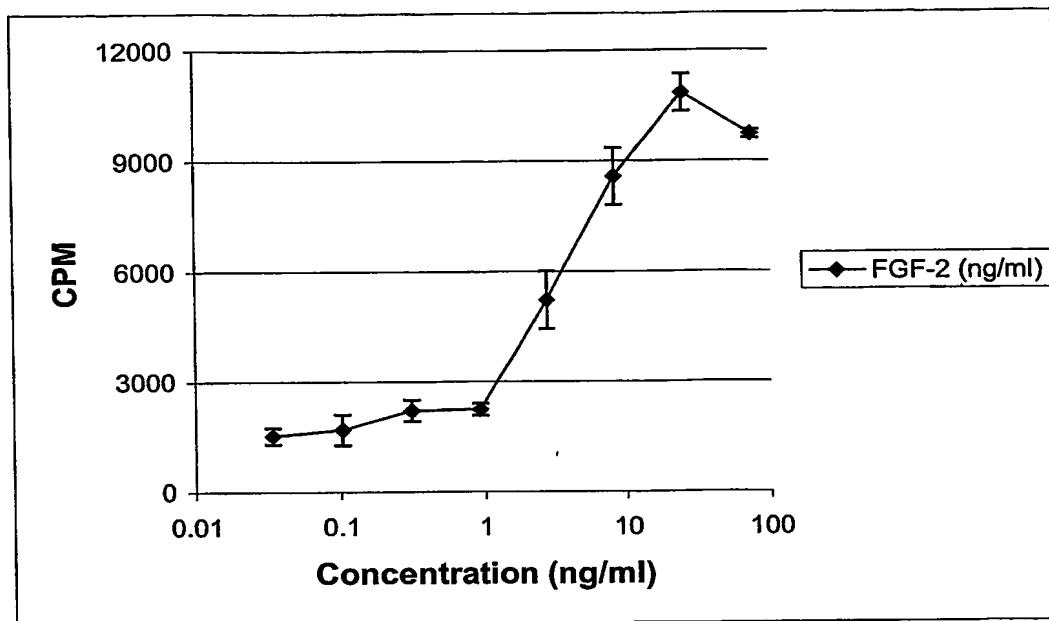


Fig. 8B

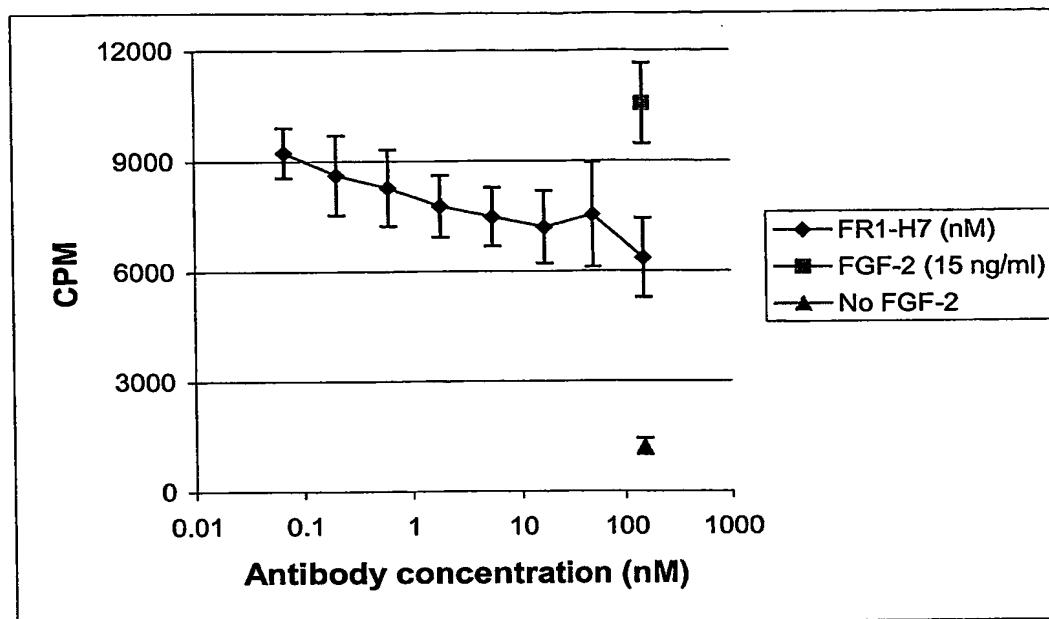
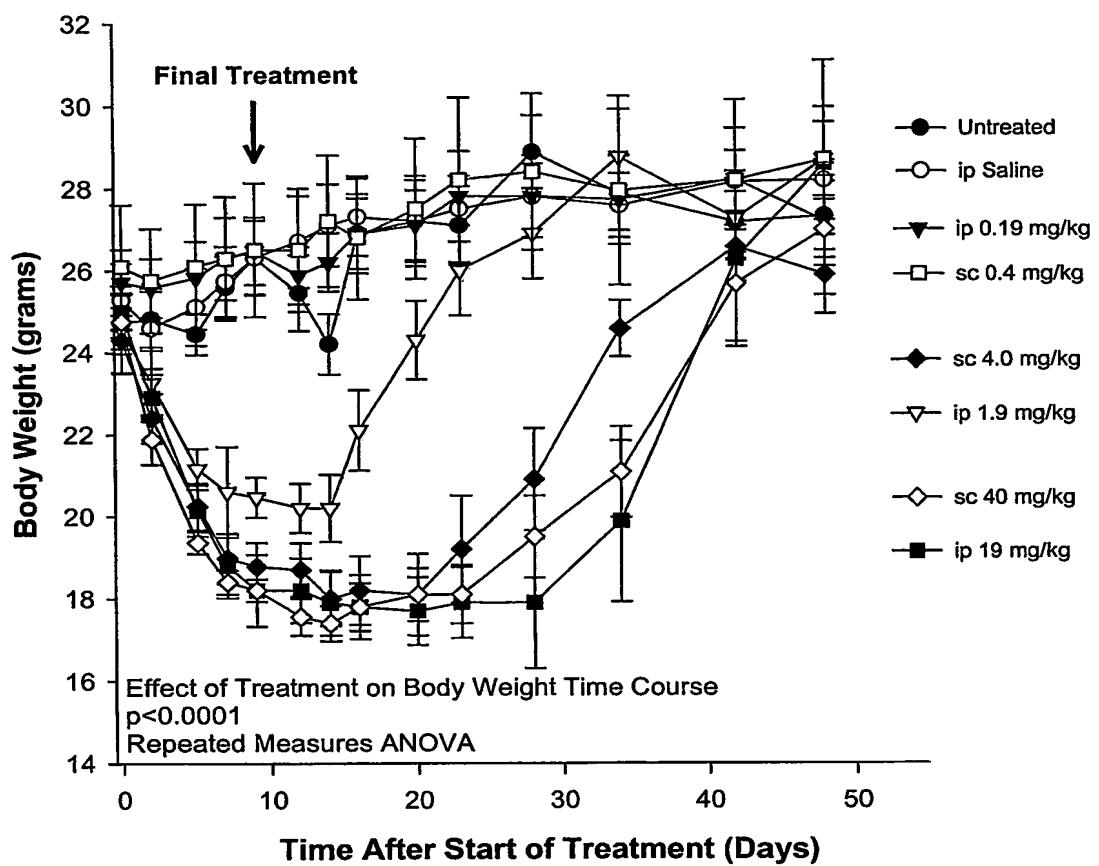


Fig. 9



*13 gram mouse euthanized

Fig. 10

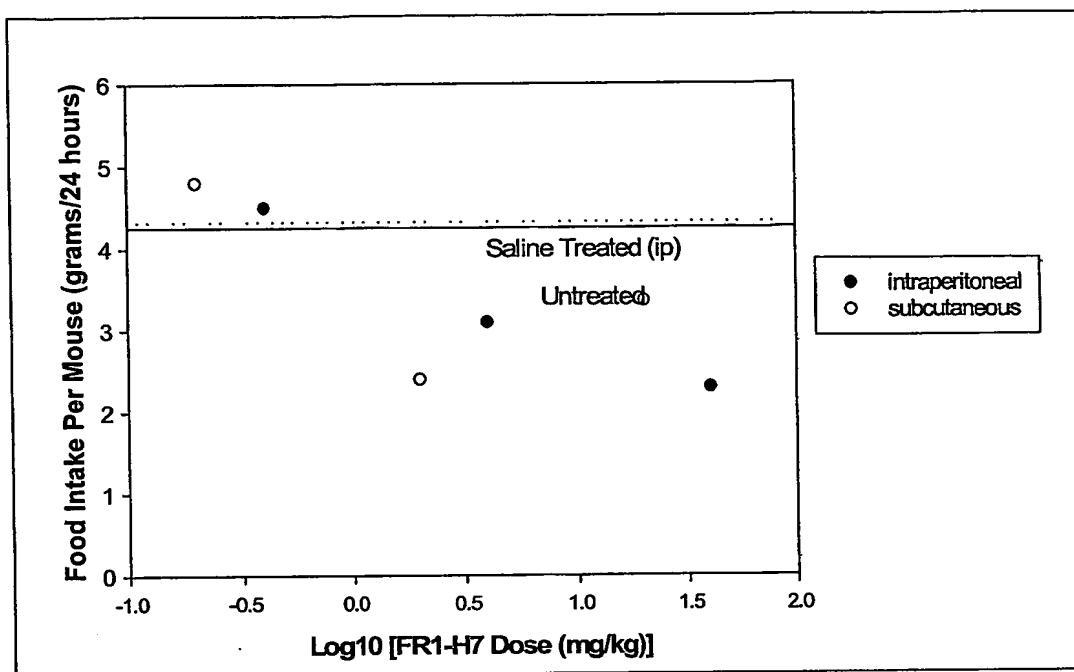


Fig. 11

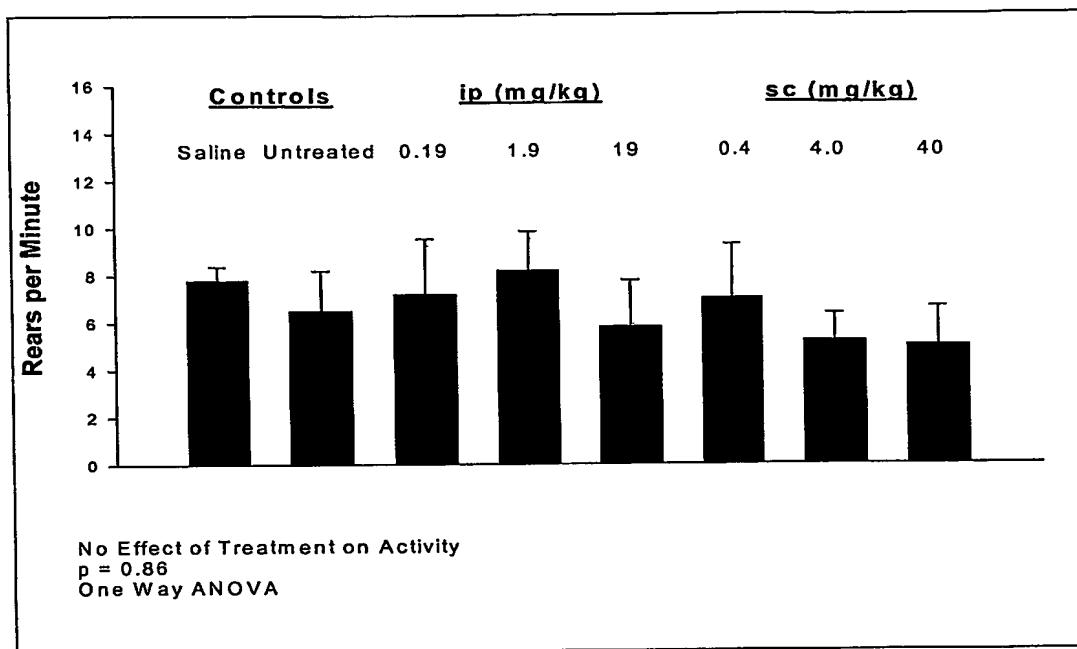


Fig. 12A

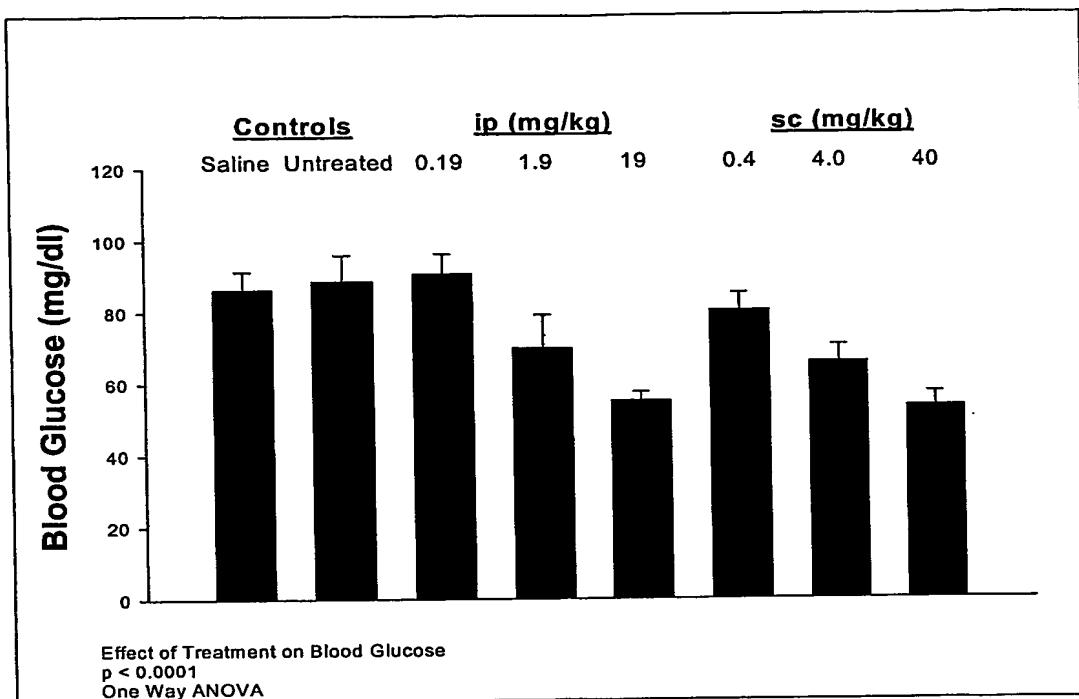


Fig. 12B

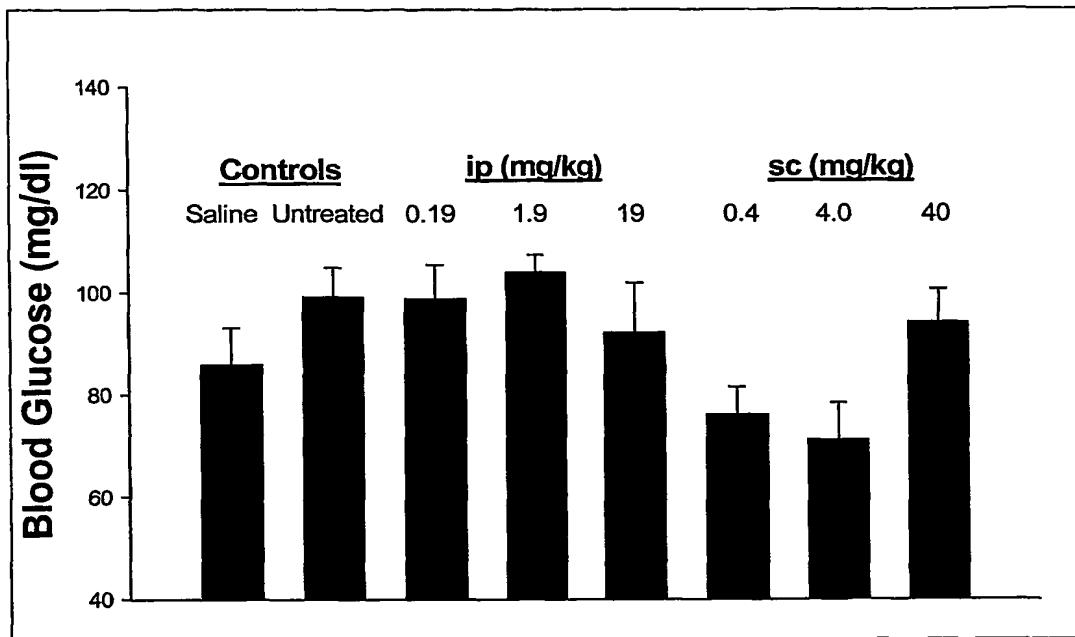


Fig. 13

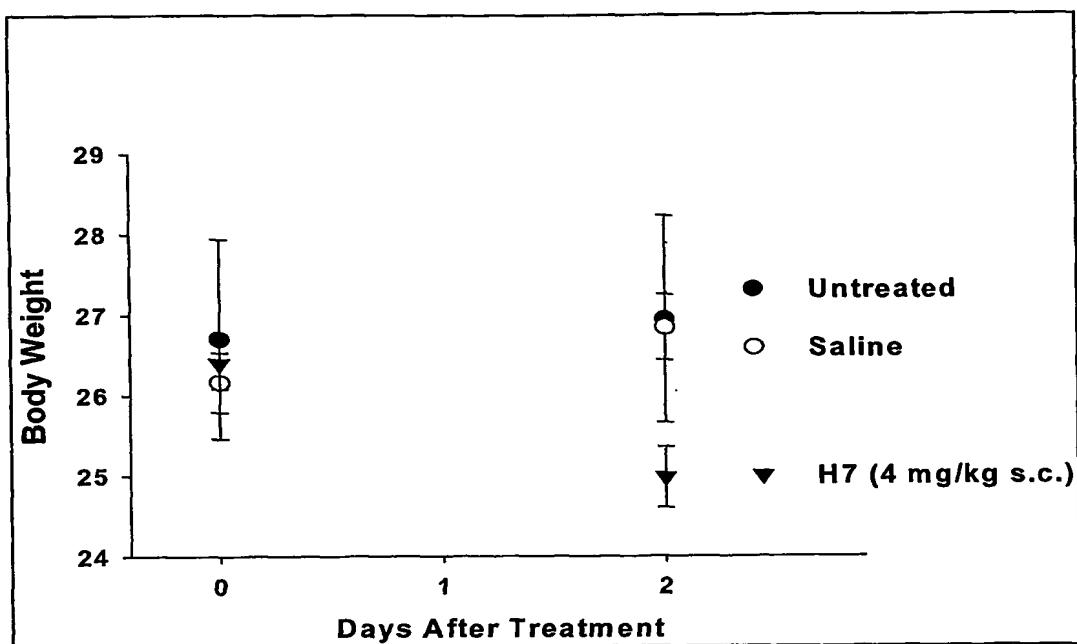


Fig. 14

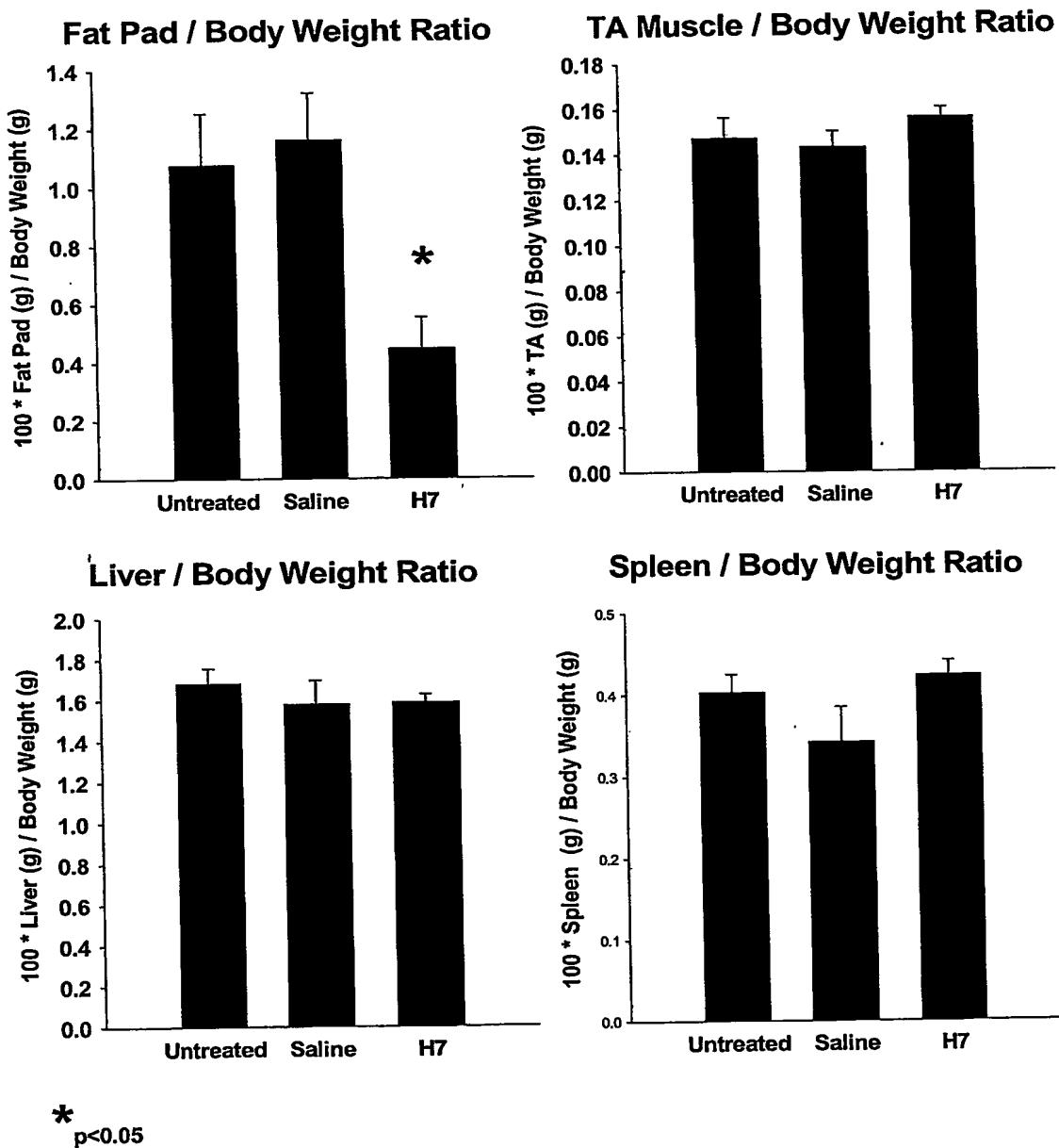


Fig. 15A

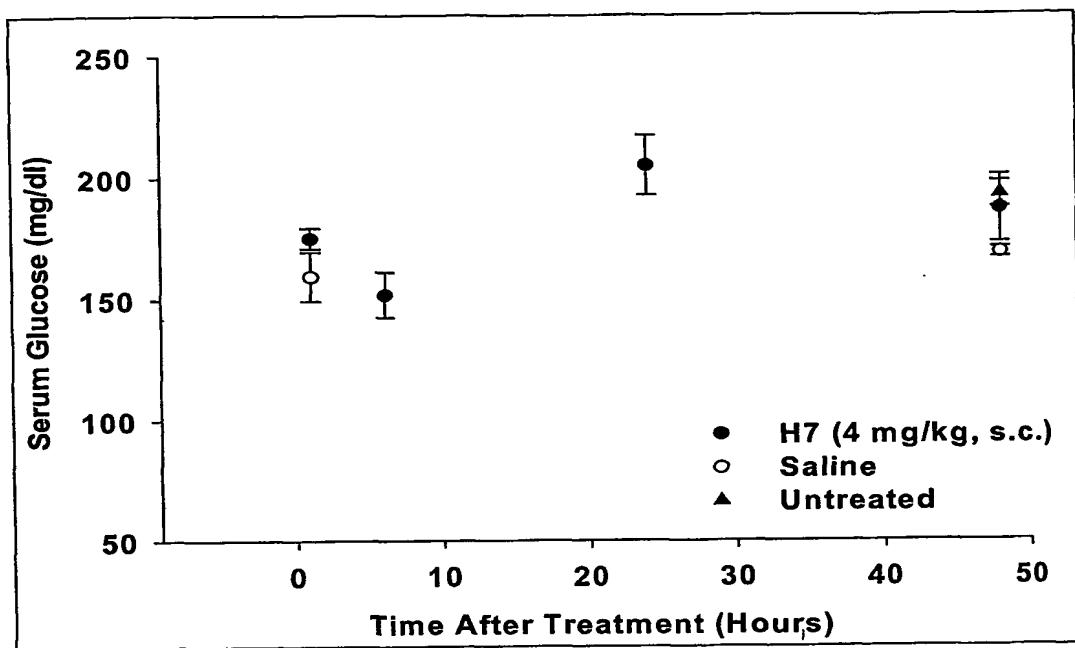


Fig. 15B

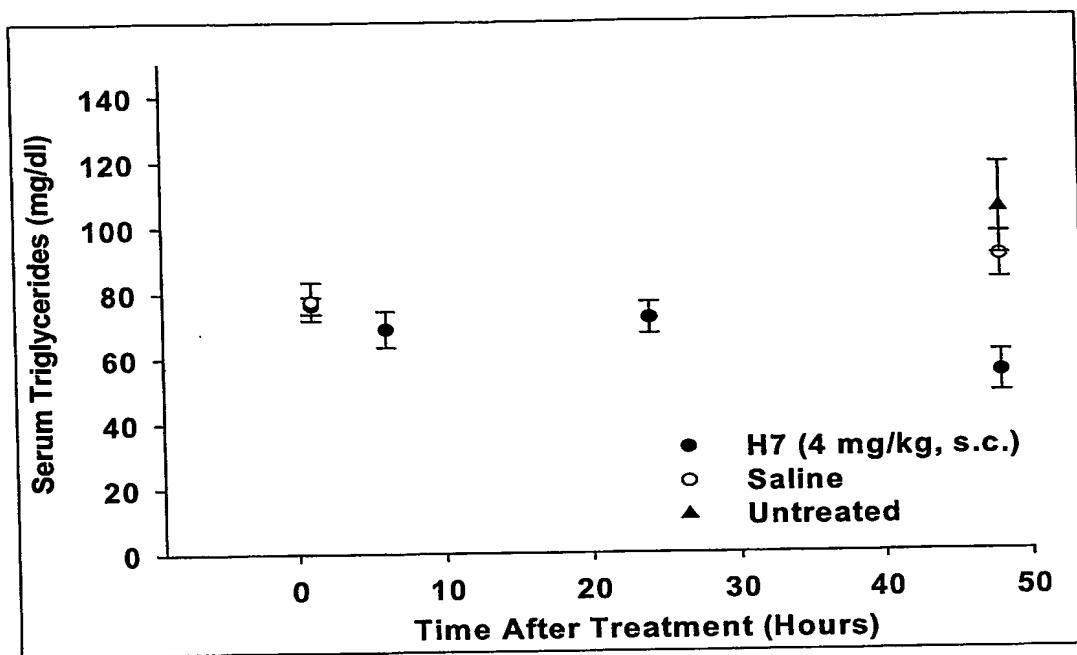


Fig. 15C

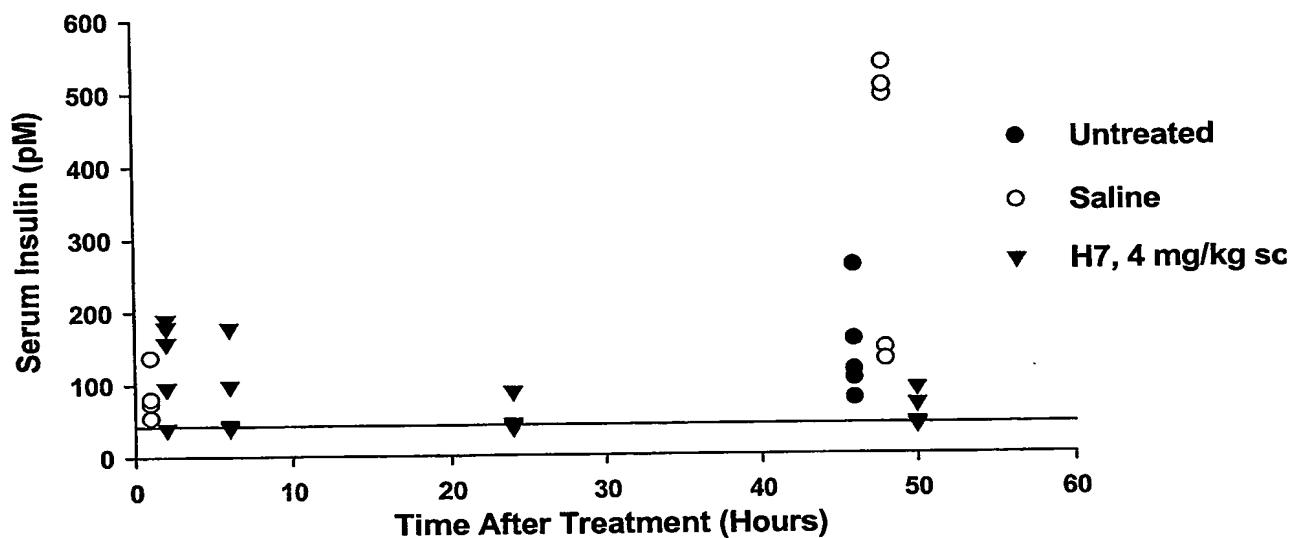


Fig. 15D

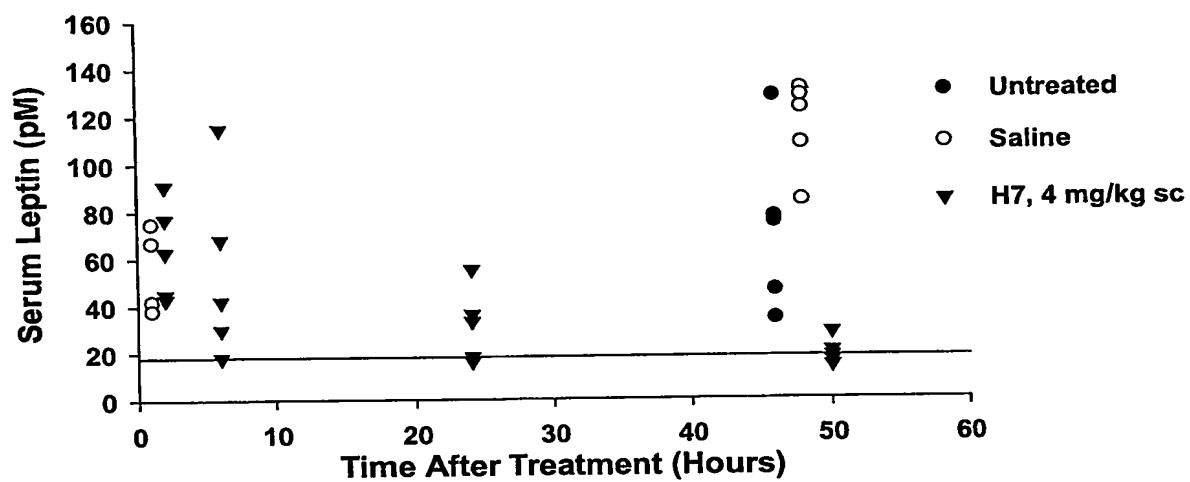


Fig. 16

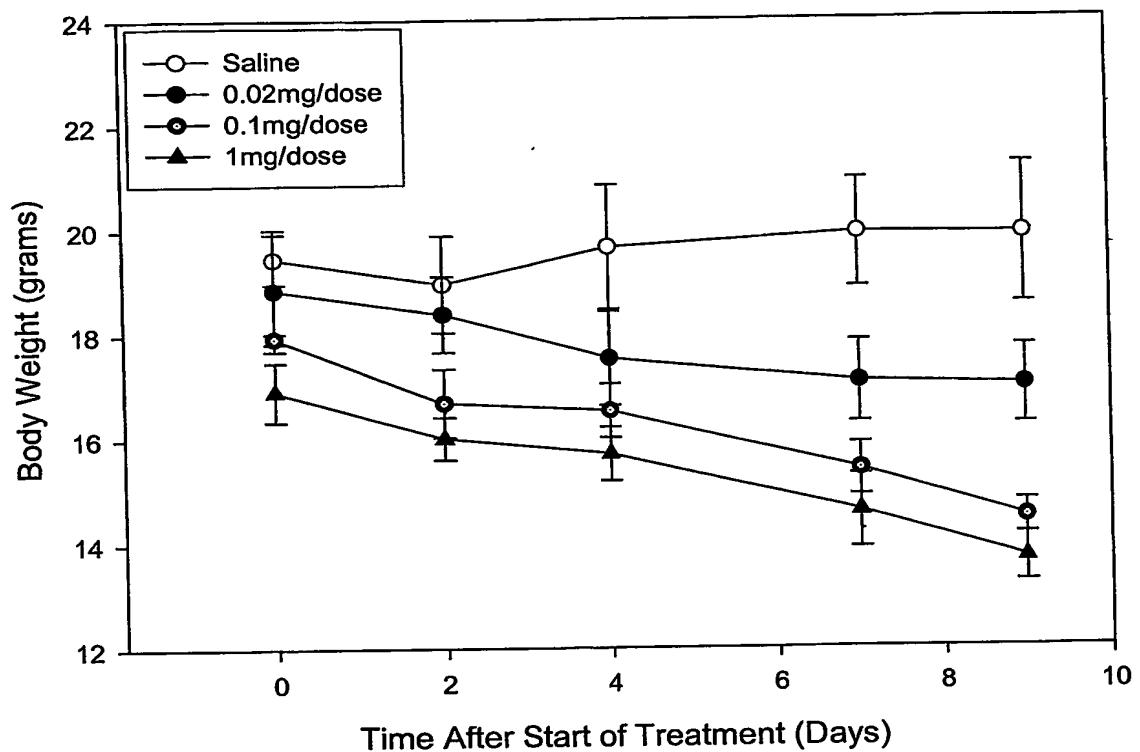


Fig. 17

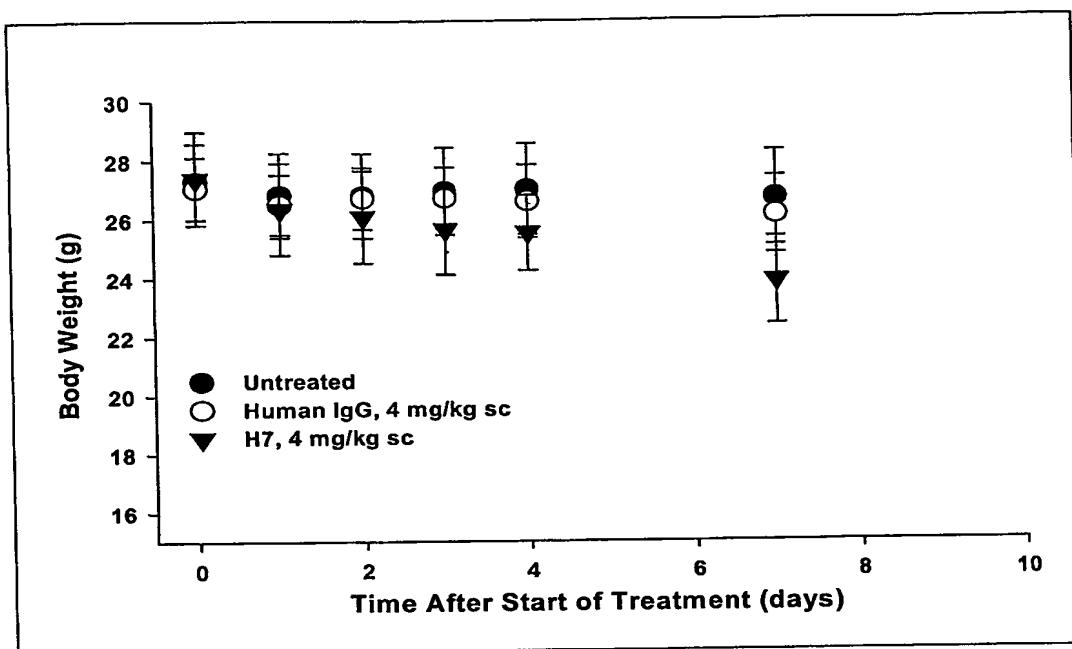


Fig. 18

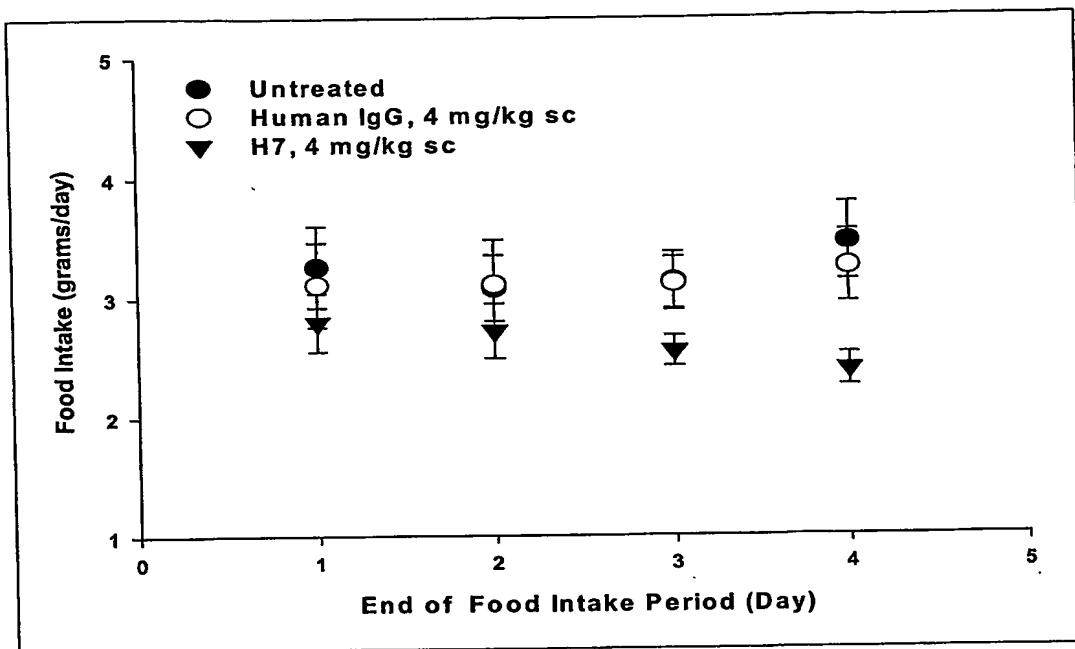


Fig. 19

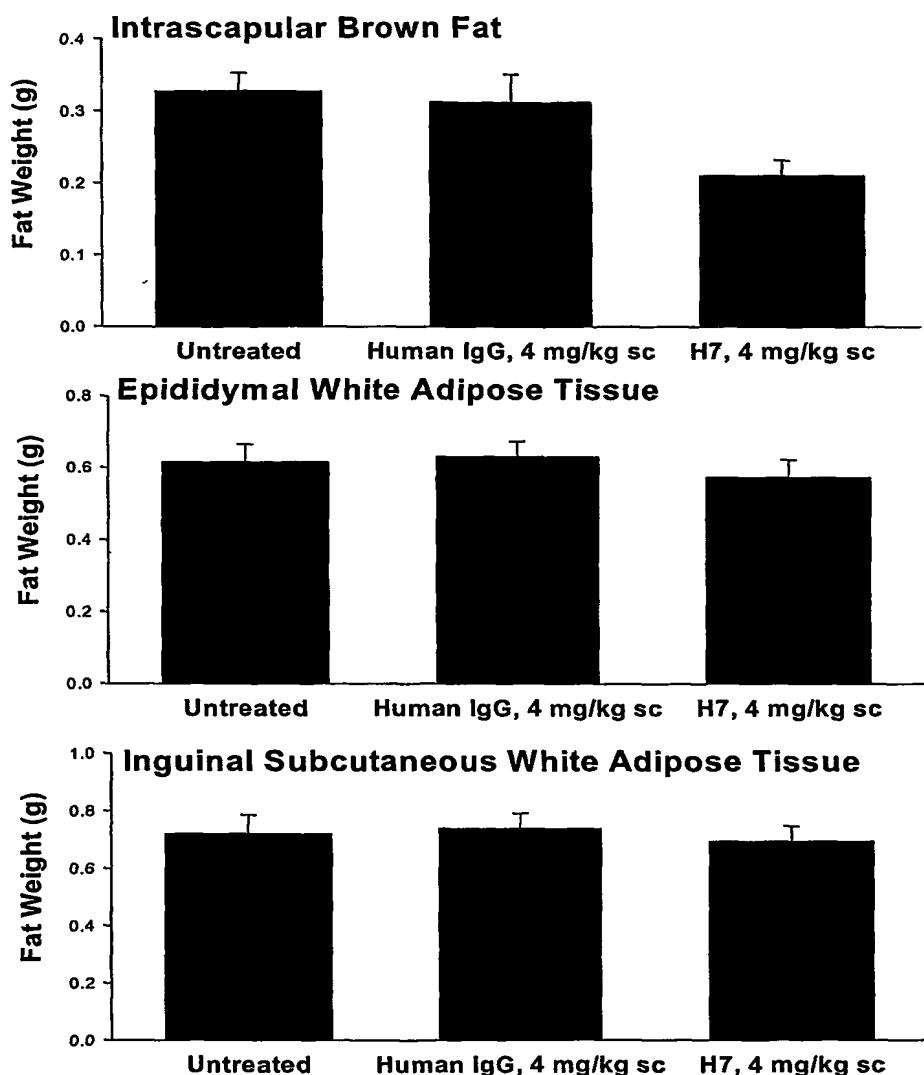


Fig. 20

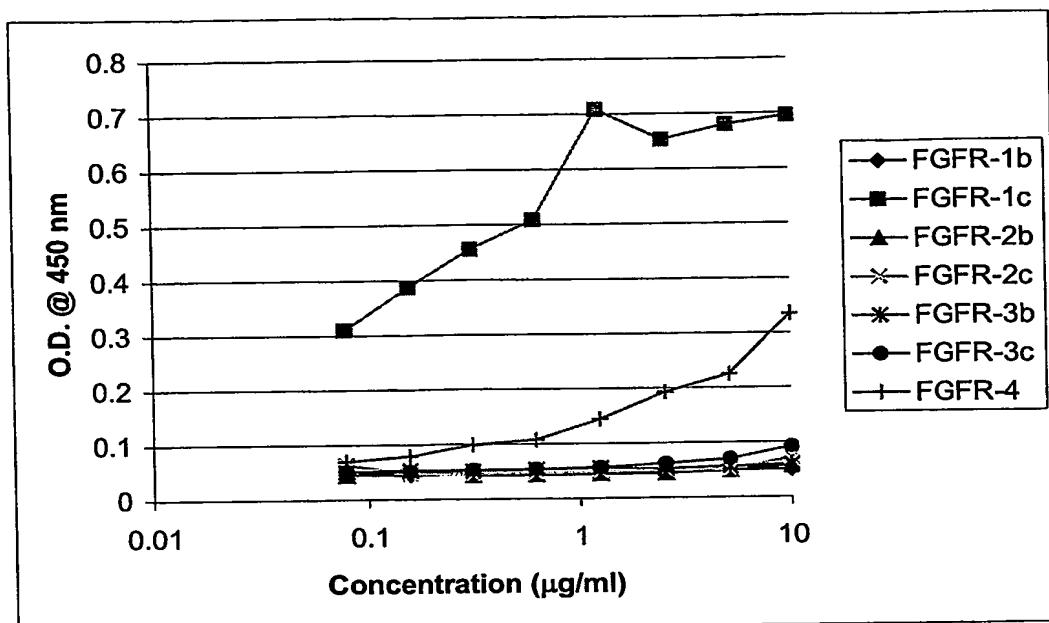


Fig. 21

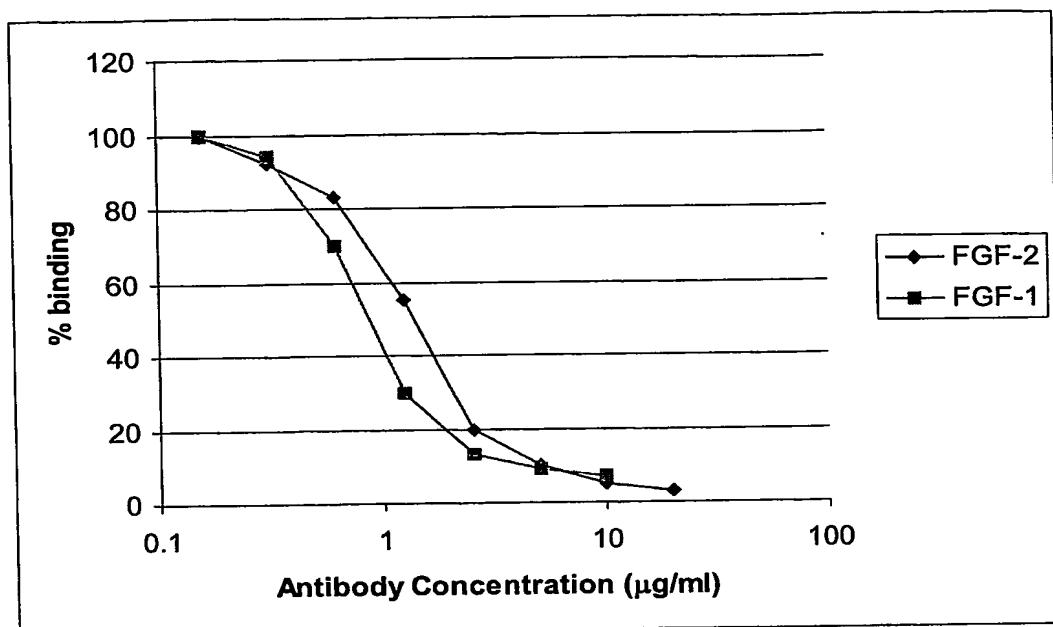


Fig. 22

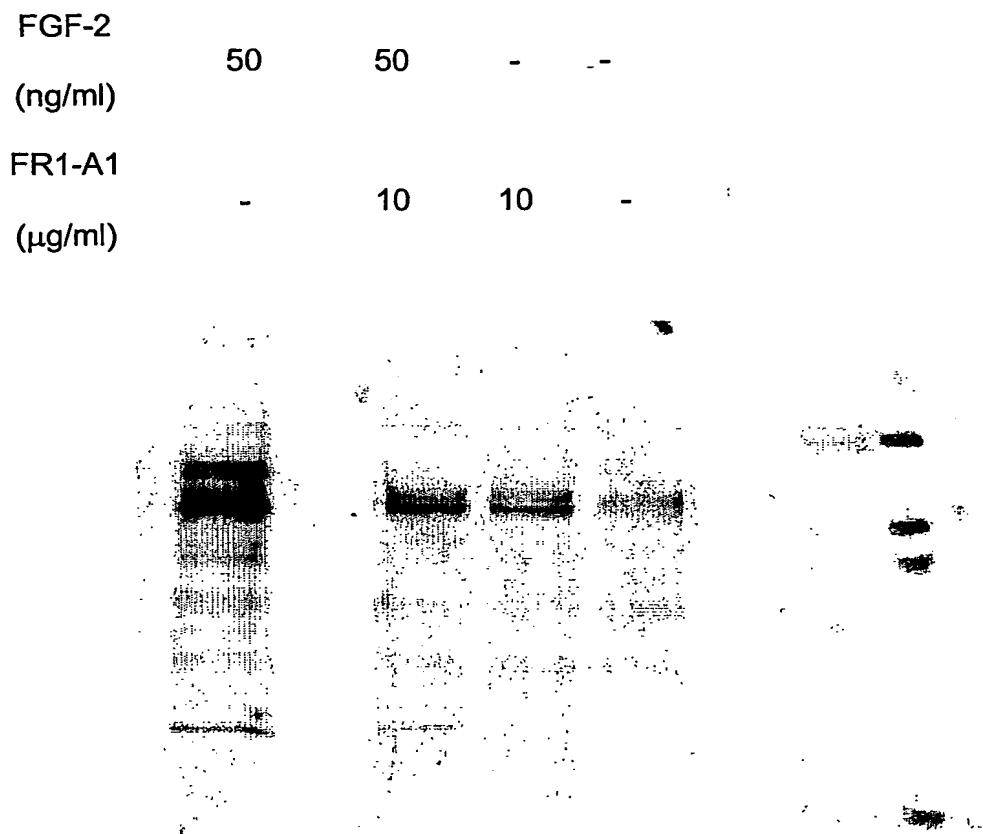


Fig. 23

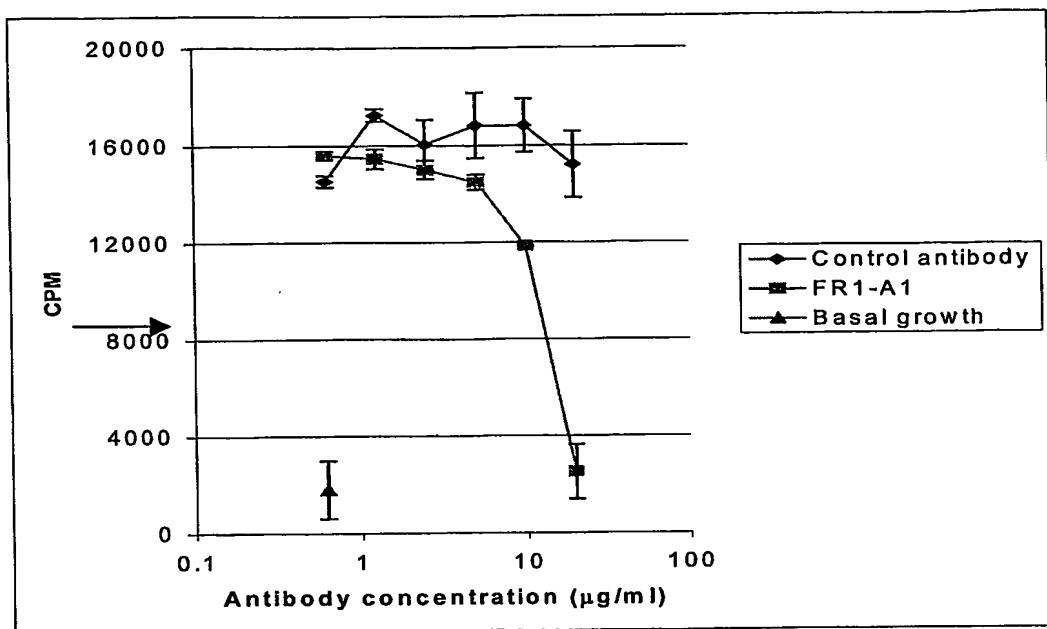


Fig. 24

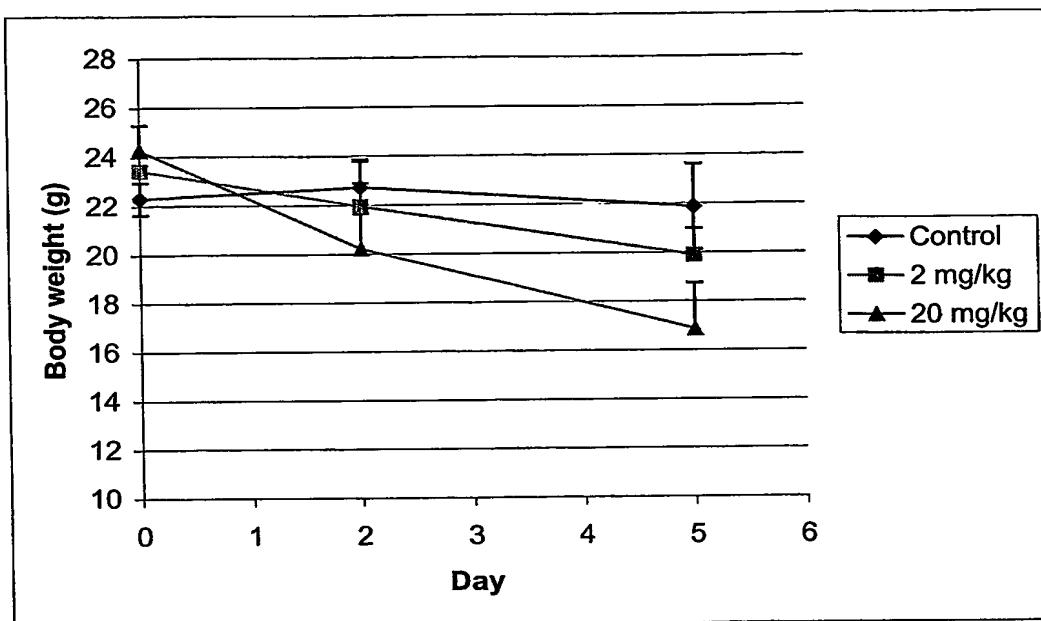


Fig .25

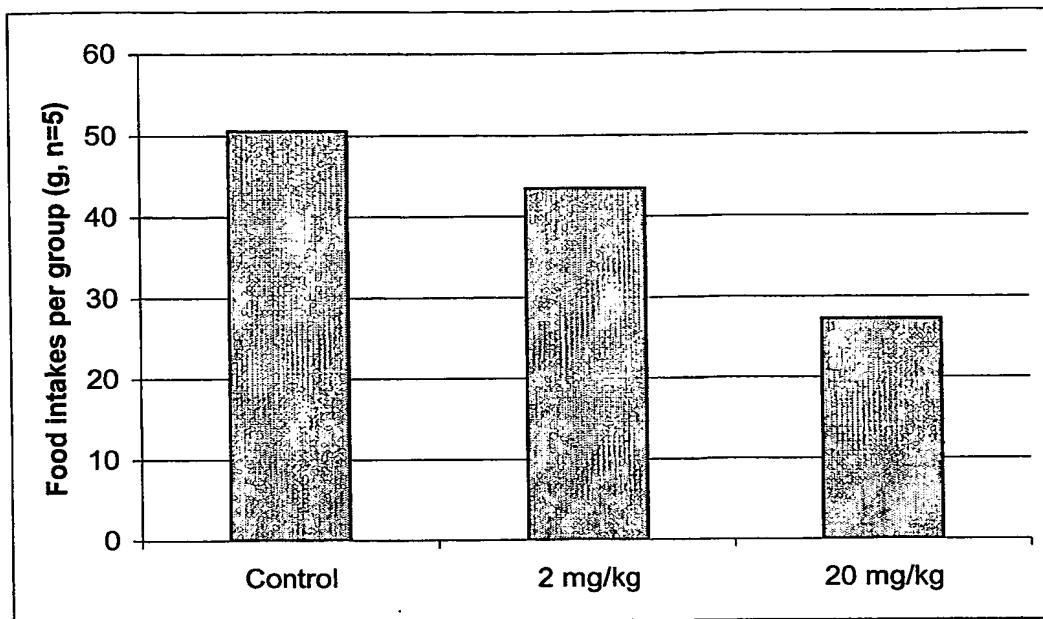


Fig. 26A

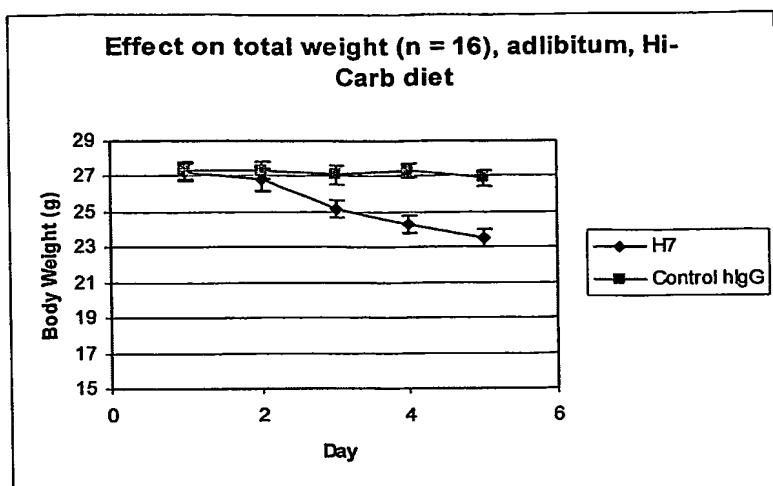


Fig. 26B

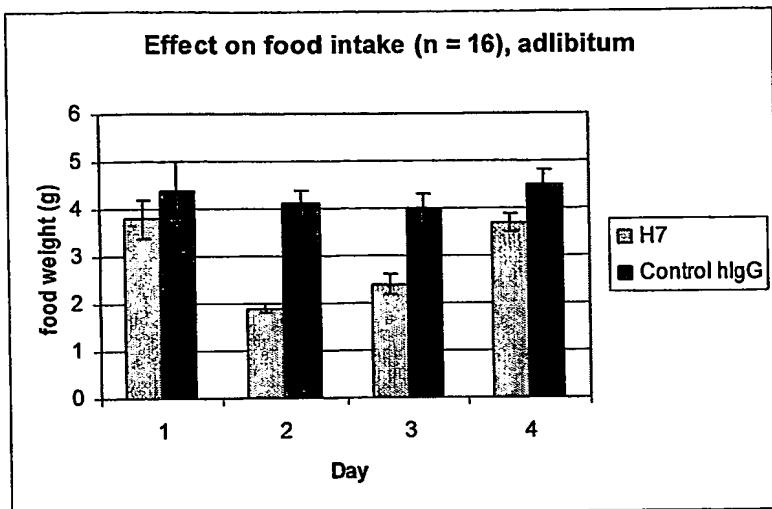


Fig 26C

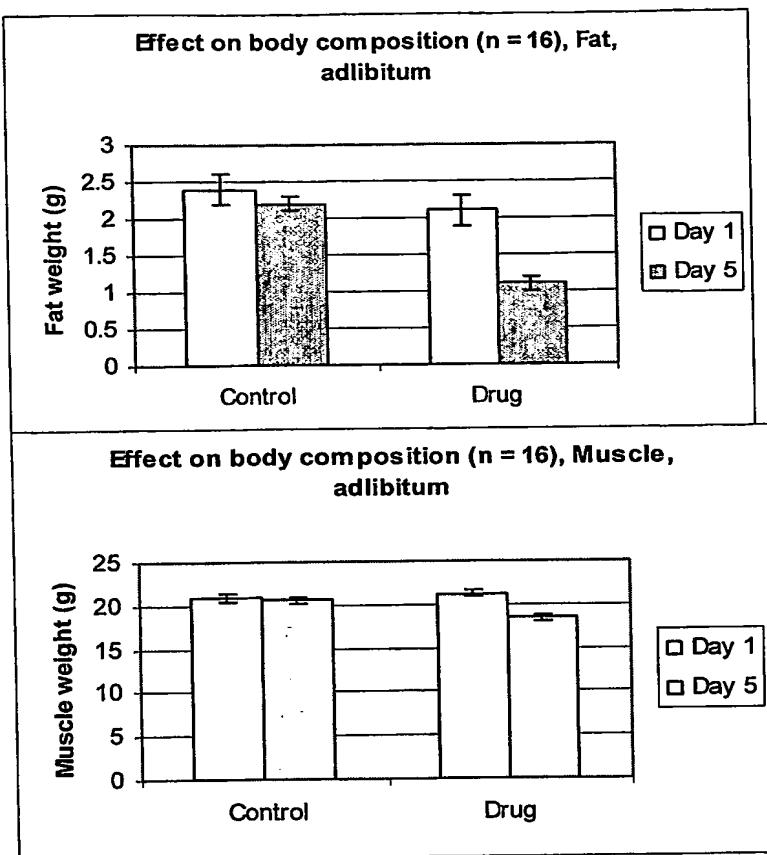


Fig. 26D

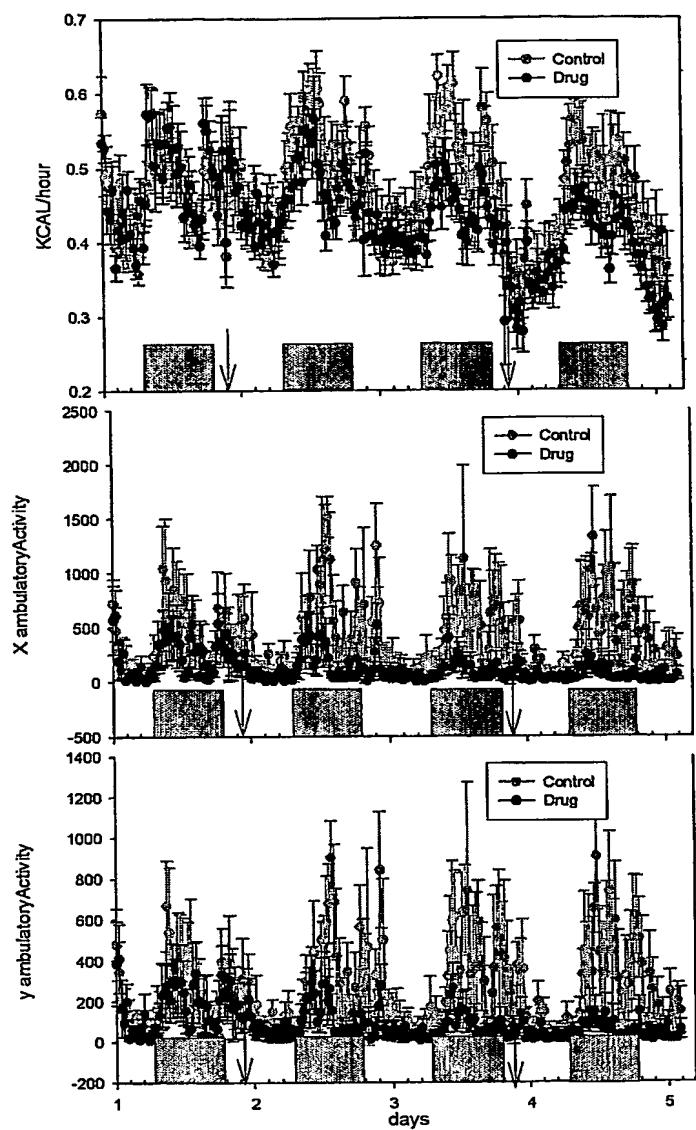


Fig. 26E

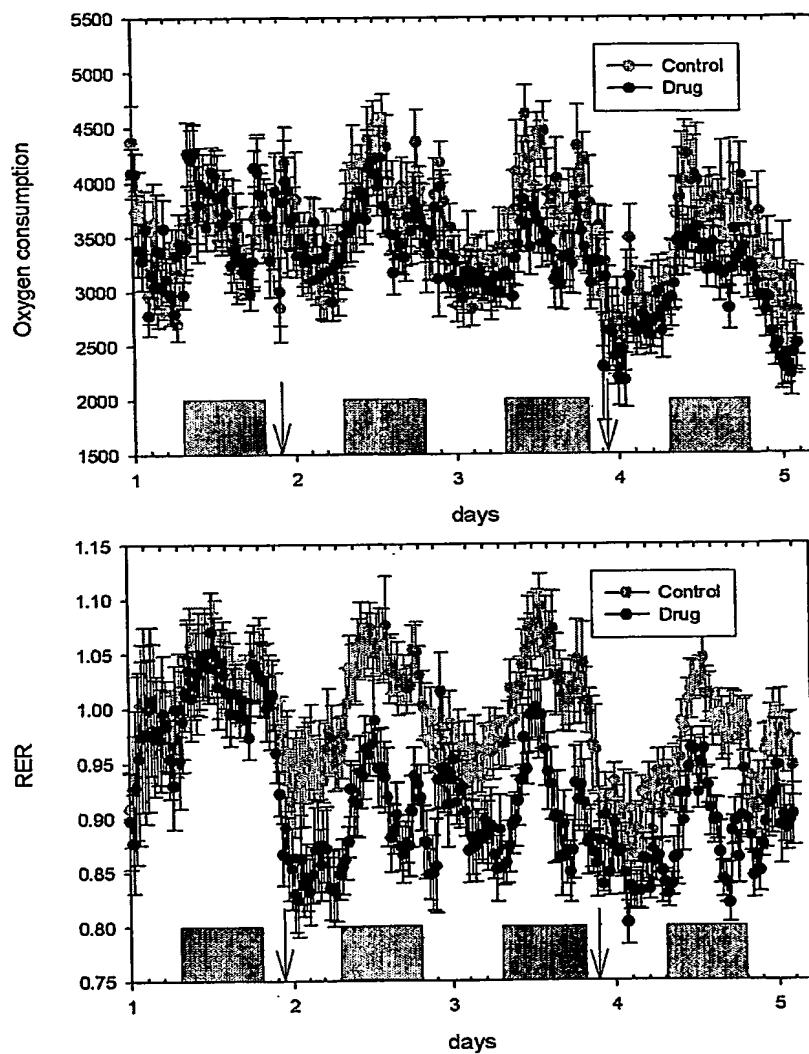


Fig. 27A

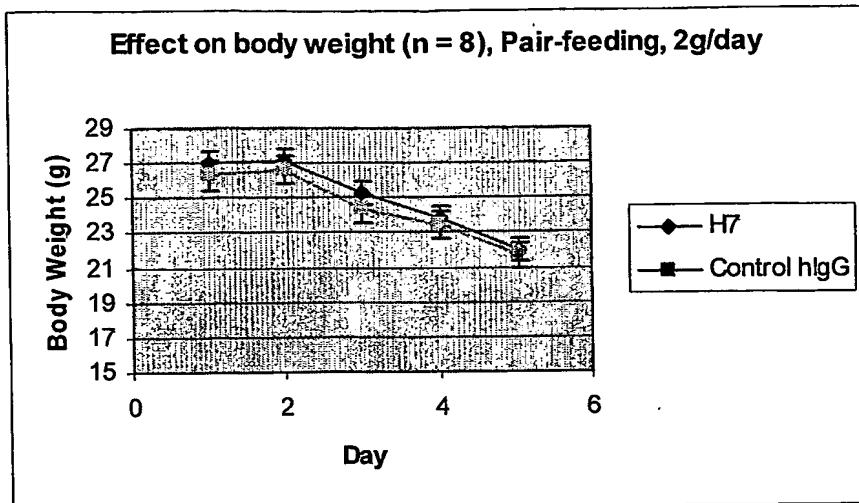


Fig. 27B

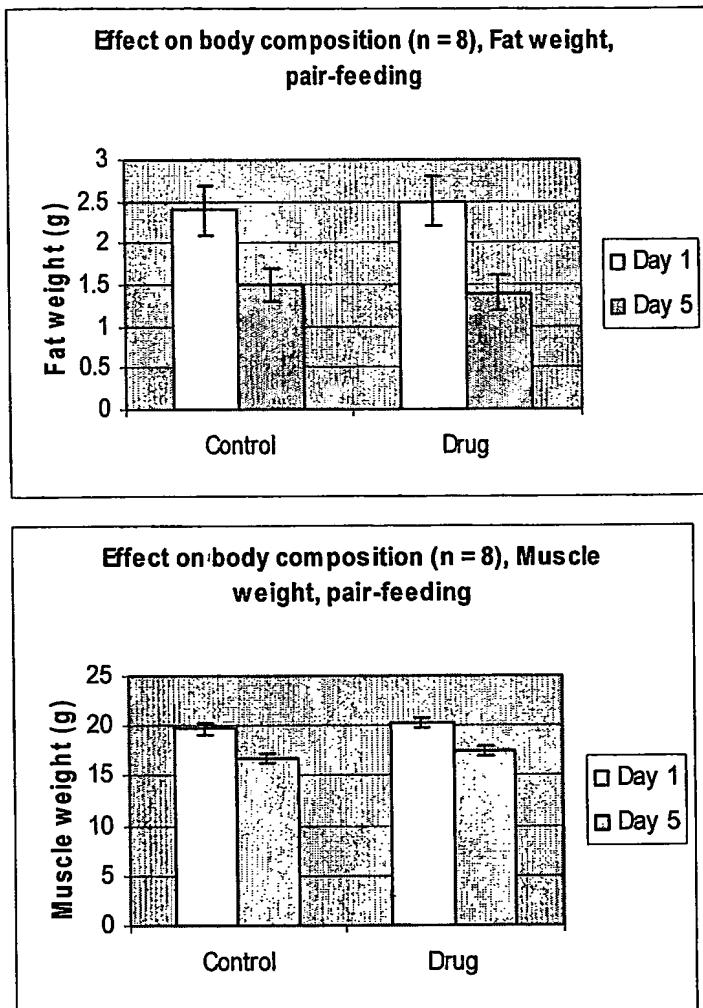


Fig. 27C

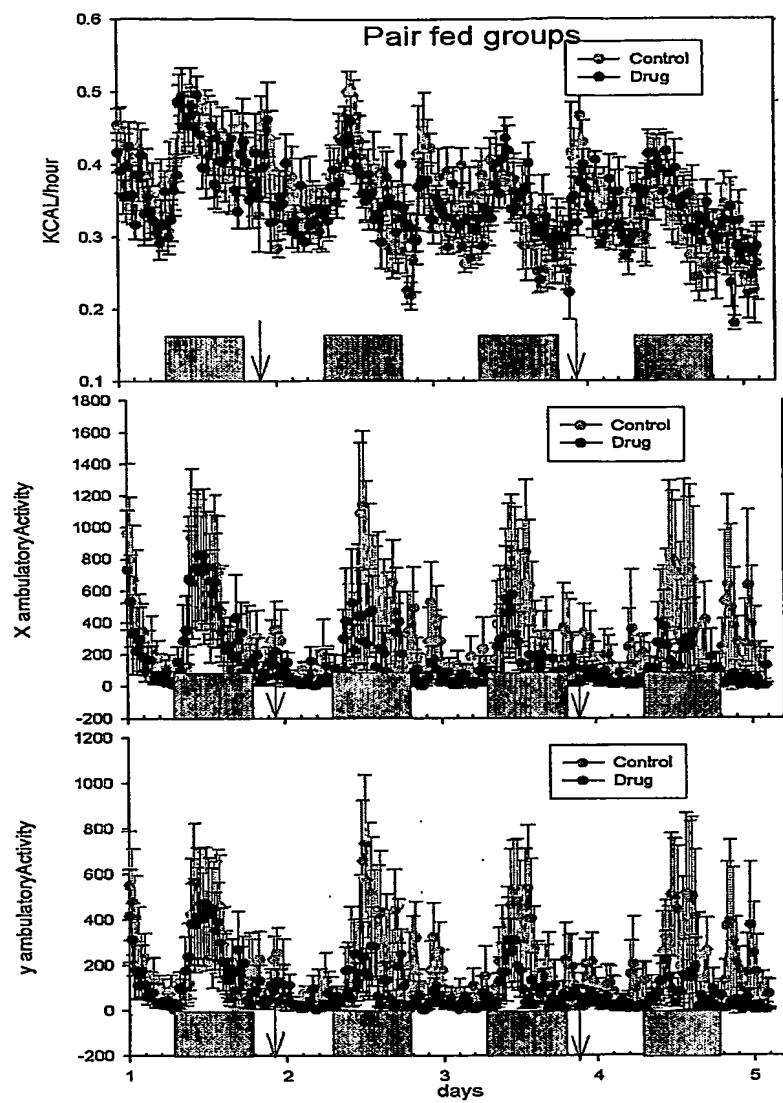


Fig. 27D

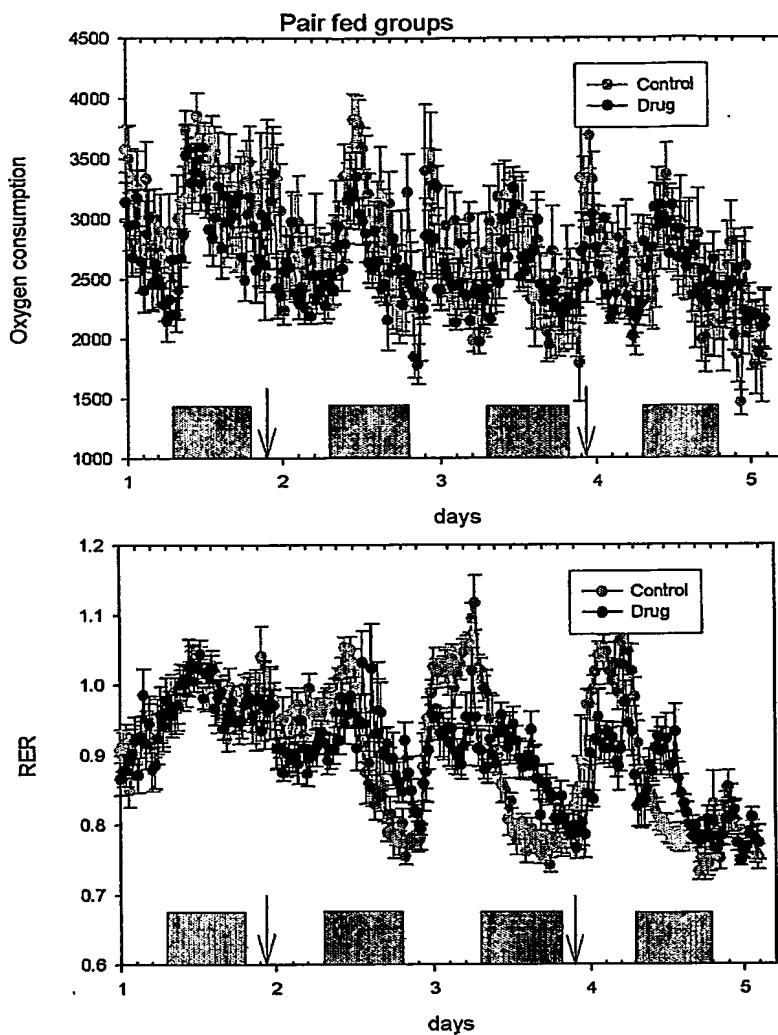


Fig. 28A. FR1-4H antibody variable sequences

Heavy chain variable region sequence (cDNA)
(gamma heavy chain)

CAGGTGCAGCTGGTGGAGTTGGCCCAGGACTGGTGAAGCCTCGGAGAC	50
CCTGTCCTCACCTGCACTGTCTCTGGCTCCATCAGTAGTTACTACT	100
GGAGCTGGATCCGGCAGCCCCAGGGAAAGGGACTGGAGTGGATTGGGTAT	150
ATCTATTACAGTGGGAGCACCAACTACAACCCCTCCCTCAAGAGTCGAGT	200
CGCCATATCAGTAGACACGTCCAAGAACCAAGCAGTTCTCCCTGAAGCTGAGCT	250
CTGTGACCGCCGCGGACACGGCCGTATTACTGTGCGAGAGAGTATTAC	300
TATGATAGTAGTGGTTATTACTTTATGCTTTGATATCTGGGCCAAGG	350
GACCACGGTCACCGTCTCAAGC	372

Heavy chain variable region sequence (amino acid)

QVQLVEFGPGLVKPSETSLTCTVSGGSISYYWSWIRQPPGKGLEWIGY	50
IYYSGSTNYNPSLKSRAVISVDTSKNQFSKLSSVTAADTAVYYCAREYY	100
YDSSGYYFYAFDIWGQGTTVTVSS	124

Light chain variable region sequence (cDNA)

CTGCCTGTGCTGACTCAGCCCCCTCAGCGTCTGGGACCCCCGGCAGAG	50
GGTCTCCATCTCTGTTCTGGAAGCAGCTCCAACATCGGAAGTAATTATG	100
TATACTGGTACCAAGCAGCTCCAGGAACGGCCCCAAACTCCTCATCTT	150
AGGAATAATCAGCGGCCCTCAGGGTCCCTGACCGATTCTCTGGCTCCAA	200
GTCTGGCACCTCAGCCTCCCTGGCCATCAGTGGGCTCCGGTCCGAGGATG	250
AGGCTGATTATTACTGTGCAGCATGGGATGACAGCCTGAGTGGTTGGGTG	300
TTCGGCGAGGGACCAAGCTGACCGTCCTAGGT	333

Light chain variable region sequence (amino acid).
(Lambda light chain)

LPVLTQPPSASGTPGQRVSISCGSSSNIGSNVYWYQQLPGTAPKLLIF	50
RNNQRPSGVPDRFSGSKSGTSASLAIISGLSEDEADYYCAAWDDSLSGWV	100
FGGGTKLTVLG	111

Fig. 28B. FR1-4H antibody variable sequence CDRs

CDR amino acid sequences

V_H:

CDR1	SYWWS
CDR2	YIYYSGSTNYNPSLKS
CDR3	EYYYDSSGYYFYAFDI

V_L:

CDR1	SGSSSNIGSNYVY
CDR2	RNNQRPS
CDR3	AAWDDSLSGWV

CDR nucleic acid sequences

V_H:

CDR1	AGTTACTACTGGAGC
CDR2	TATATCTATTACAGTGGGAGCACCAACTACAACCCCTCCCTCAAGAGT
CDR3	GAGTATTACTATGATAAGTAGTGGTTATTACTTTATGCTTTGATATC

V_L:

CDR1	TCTGGAAAGCAGCTCCAACATCGGAAGTAATTATGTATAC
CDR2	AGGAATAATCAGCGGCCCTCA
CDR3	GCAGCATGGGATGACAGCCTGAGTGGTTGGGTG

Fig. 29

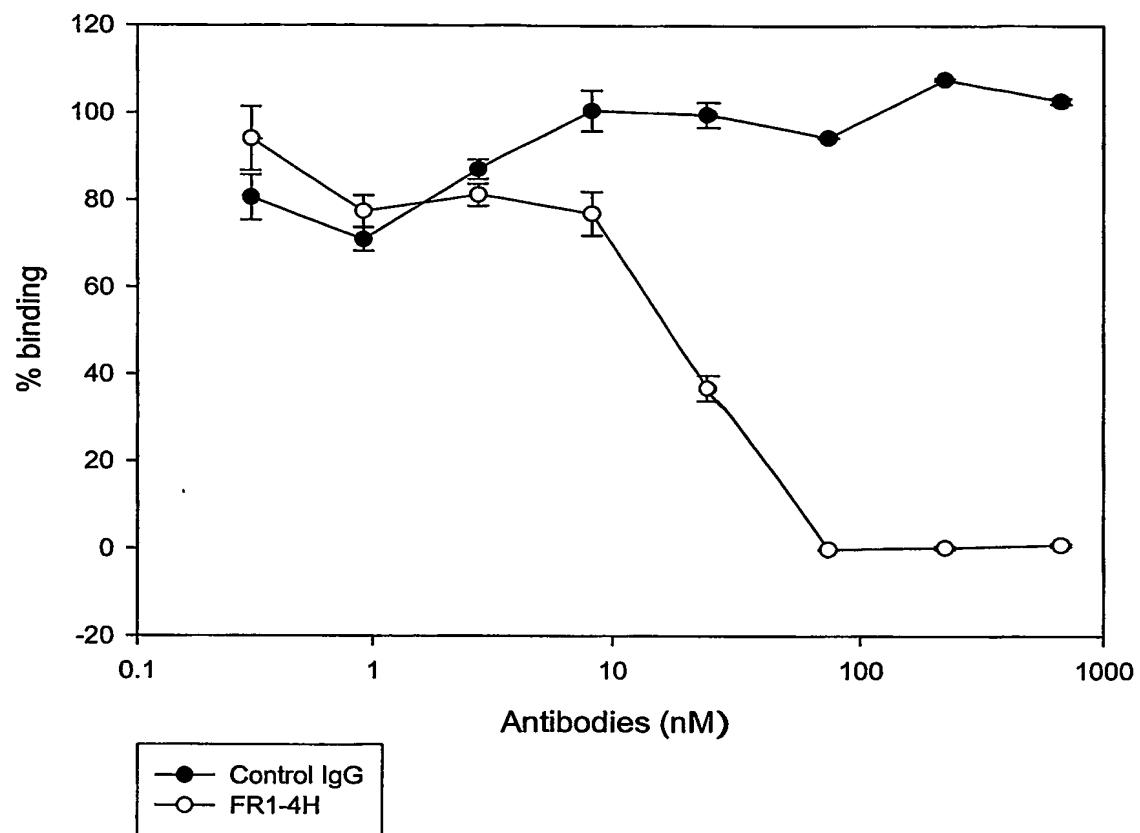
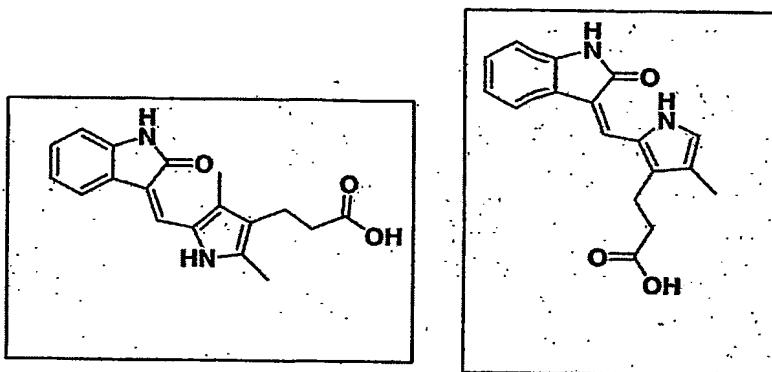
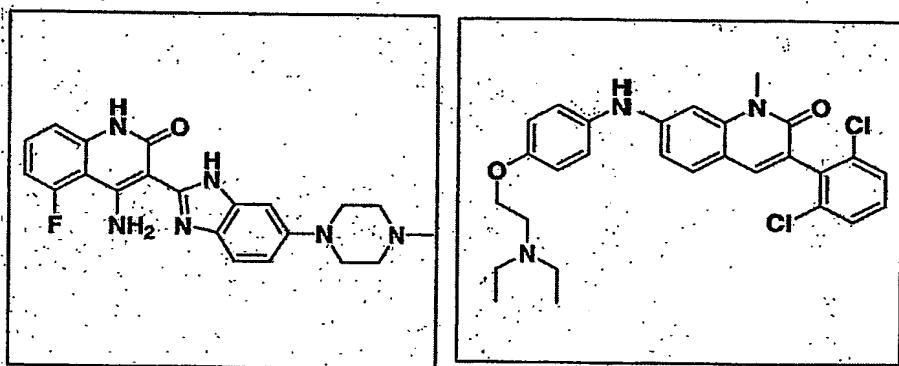


Fig. 30. Examples of FGFR small molecule inhibitors.

Indolinone derivatives:



Quinolinone derivatives:



Pyrimido-pyridine derivatives:

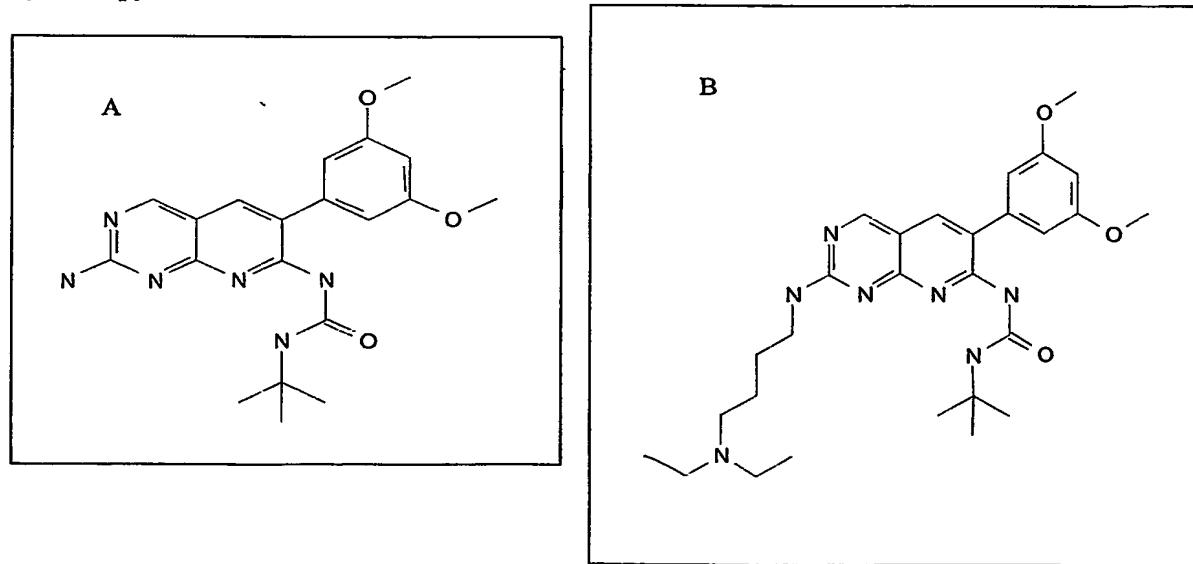
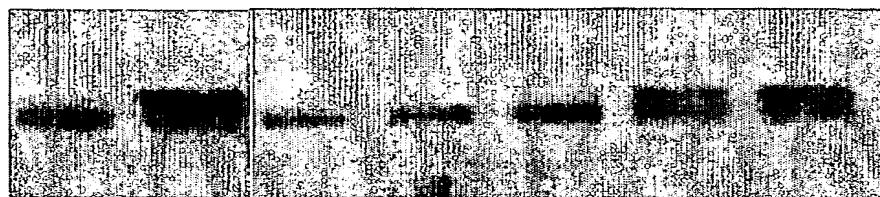


Fig. 31.

FGF	-	5 ng	5 ng	5 ng	5 ng	5 ng	5 ng
Pryimido-pyridines derivative A	-	-	0.5 μ M	0.2 μ M	0.1 μ M	0.05 μ M	0.02 μ M



FGF	-	100 ng	100 ng	100 ng	100 ng
Pryimido-pyridines derivative B	-	-	0.1 μ M	0.03 μ M	0.01 μ M

